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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,951	01/11/2002	Leonid Beigelman	MBHB00,716-D (RPI No. 600)	7085
20306	7590	03/23/2004	EXAMINER	
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			LEWIS, PATRICK T	
			ART UNIT	PAPER NUMBER
			1623	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/043,951

Applicant(s)

BEIGELMAN ET AL.

Examiner

Patrick T. Lewis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's Response dated December 29, 2003

1. In the Response filed December 29, 2003, claims 1-2 were amended. Applicant presented arguments directed to the rejection of claims 1-26 under 35 U.S.C. 112, second paragraph; the rejection of claims 1-8, 11-18, and 24-26 under 35 U.S.C. 102(b) as being anticipated by Tang et al. J. Org. Chem., 1999, Vol. 64, pages 747-754 (Tang); and the rejection of claims 1-45 under 35 U.S.C. 103(a) as being unpatentable over the combination of Tang et al. J. Org. Chem., 1999, Vol. 64, pages 747-754 (Tang) and Usman et al. J. Am. Chem. Soc. 1987, Vol. 109, pages 7845-7854 (Usman).
2. Claims 1-45 are pending. An action on the merits of claims 1-45 is contained herein below.
3. The rejection of claims 1-26 under 35 U.S.C. 112, second paragraph, has been rendered moot in view of applicant's amendments dated December 29, 2003.
4. The rejection of claims 1-8, 11-18, and 24-26 under 35 U.S.C. 102(b) as being anticipated by Tang et al. J. Org. Chem., 1999, Vol. 64, pages 747-754 (Tang) has been rendered moot in view of applicant's amendments dated December 29, 2003.
5. Applicant's arguments with respect to the rejection of claims 1-45 under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Tang et al. *J. Org. Chem.*, 1999, Vol. 64, pages 747-754 (Tang); Usman

et al. *J. Am. Chem. Soc.* 1987, Vol. 109, pages 7845-7854 (Usman); and Gundlach et al. *Tetrahedron Letters* (1997), Vol. 38, pages 4039-4042 (Gundlach).

Claims 1-45 are drawn to a method for synthesizing an unbranched 2'-O-silyl-nucleoside phosphoramidite comprising:

- a) introducing a 5',3'-cyclic silyl protecting group to a nucleoside;
- b) introducing a 2'-O-silyl protecting group to the product from (a);
- c) selectively desilylating the product from (b);
- d) introducing a 5'-hydroxyl protecting group to the product from (c);
- e) introducing a phosphoramidite moiety at the 3'-position of the product from (d),
- and
- f) optionally introducing a nucleic acid base protection group if necessary to the nucleoside before step (a) or after step (b).

Tang teaches a method for the synthesis of phosphoramidite derivatives of 2'-C- β -methylcytidine (page 748, Scheme 1). The method of Tang comprises a) introduction of a nucleic base-protected nucleoside; b) 5',3'-cyclic silyl protection of the nucleoside using *t*-Bu₂SiCl₂; c) protection of the 2'-hydroxyl using *t*-BuMe₂SiOTf; d) selective removal of the 5',3'-cyclic silyl protective group using HF-pyridine; e) protection of the 5'-hydroxyl using DMTrCl; and f) the introduction of a 3'-O-(2-cyanoethyl-N,N-diisopropylphosphoramidite) moiety.

Tang differs from the instantly claimed invention in that: 1) Tang does not teach the protection of the nucleic base after step (b); 2) Tang only teaches the use of methylcytidine as the nucleoside; 3) Tang does not teach the synthesis of unbranched

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nucleoside; and 4) Tang does not teach the introduction of a 2'-O-triisopropylsilyloxymethyl protecting group.

Gundlach teaches an analogous process to Tang (page 4041, Scheme 2). Gundlach and Tang differ in that Gundlach employs a different base moiety and the nucleoside moiety does not contain a 2'-methyl group.

Usman teaches the automated chemical synthesis of oligonucleotides using 2'-O-silylated ribonucleoside 3'-O-phosphoramidites. Usman teaches using both TBDMS and TIPS as the 2'-O-protective group for ribonucleoside phosphoramidites (page 7846, Scheme I). Usman further teaches using various nucleic acid bases.

It would have been obvious to one of ordinary skill in the art at the time of the invention to protect the nucleic acid base after step (b) since Tang teaches of the steps employed in the instantly claimed method including protection of nucleic acid base. Merely reversing the order of the steps of a multi-step process does not impart patentability when no unexpected result is obtained. *Ex parte Rubin* (POBA 1959) 128 USPQ 440; *Cohn v. Comr. Pats.* (DCDC 1966) 251 Fsupp 437, 148 USPQ 486. It would have also been obvious to one of ordinary skill in the art to employ unbranched nucleosides [no 2'-methyl] in the method of Tang as the prior art teaches the synthesis of 2'-O-silyl-nucleoside phosphoramidites branched or unbranched nucleosides (see Gundlach). The practice of the instantly claimed invention using a nucleic acid base moiety other than methylcytidine and the selection of appropriate silyl-protecting groups is seen to be within the purview of the skilled artisan as demonstrated by Usman. One

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would have been motivated to do so in order to produce analogues useful to regulate gene expression by antisense or ribozyme cleavage approaches.

Conclusion

10. Claims 1-45 are pending. Claims 1-45 are rejected. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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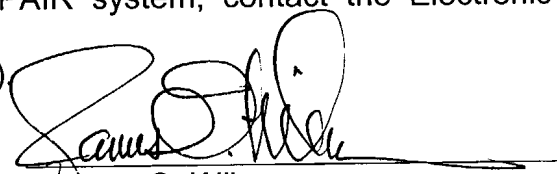
Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623



James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

ptl
March 20, 2004